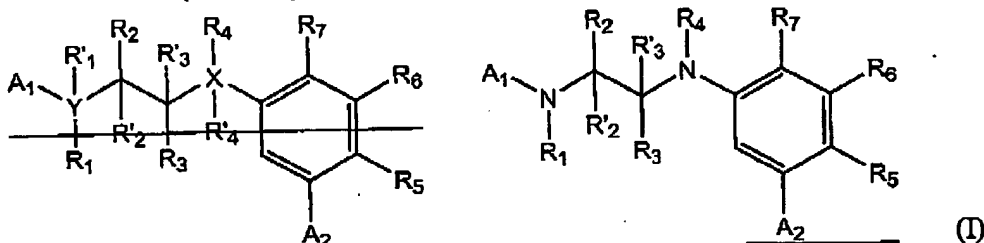


AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A compound having the structure:



wherein:

~~X and Y are independently selected from the group consisting of nitrogen, oxygen, and optionally substituted carbon;~~

A<sub>1</sub> and A<sub>2</sub> are optionally substituted aryl, arylamino, aryloxy or heteroaryl;

R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> are independently selected from the group consisting of hydrogen, hydroxyl, and optionally substituted loweralkyl, cycloloweralkyl, alkylaminoalkyl, loweralkoxy, amino, alkylamino, alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, heteroaralkylcarbonyl, aryl and heteroaryl;

[[R'<sub>1</sub>, R'<sub>2</sub>,]] R'<sub>2</sub> and R'<sub>3</sub> [[and R'<sub>4</sub>]] are independently selected from the group consisting of hydrogen, and optionally substituted loweralkyl;

R<sub>5</sub>, R<sub>6</sub> and R<sub>7</sub> are independently selected from the group consisting of hydrogen, hydroxy, halo, carboxyl, nitro, amino, amido, amidino, imido, cyano, and substituted or unsubstituted loweralkyl, loweralkoxy, alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, heteroaralkylcarbonyl, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkylaminocarbonyloxy, arylaminocarbonyloxy, formyl, loweralkylcarbonyl, loweralkoxycarbonyl, aminocarbonyl, aminoaryl, alkylsulfonyl, sulfonamido, aminoalkoxy, alkylamino, arylamino, aralkylamino, heteroarylamino, heteroaralkylamino, alkylcarbonylamino, alkylaminocarbonylamino, arylaminocarbonylamino, aralkylcarbonylamino, heteroaralkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, amidino, cycloalkyl, cycloamido, cyclothioamido, cycloamidino,

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1420 Fifth Avenue  
Suite 2800  
Seattle, Washington 98101  
206.682.8100

heterocyclyl, heterocycloamidino, cycloimido, heterocycloimido, guanidinyl, aryl, biaryl, heteroaryl, heterobiaryl, heterocyclo, heterocycloalkyl, arylsulfonyl and arylsulfonamido; and the pharmaceutically acceptable salts thereof.

2-5. (Canceled)

6. (Original) A compound of claim 1, wherein at least one of A<sub>1</sub> and A<sub>2</sub> comprises an aromatic ring having from 3 to 10 carbon ring atoms and optionally 1 or more ring heteroatoms.

7. (Original) A compound of claim 6, wherein at least one of A<sub>1</sub> and A<sub>2</sub> is optionally substituted carbocyclic aryl, arylamino or aryloxy.

8. (Original) A compound of claim 6, wherein at least one of A<sub>1</sub> and A<sub>2</sub> is optionally substituted heteroaryl.

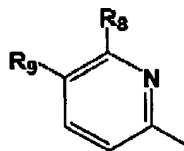
9. (Original) A compound of claim 6, wherein at least one of A<sub>1</sub> and A<sub>2</sub> is selected from the group consisting of substituted or unsubstituted phenyl, phenylamino, phenyloxy, pyridyl, pyrimidinyl, thiazolyl, indolyl, imidazolyl, oxadiazolyl, tetrazolyl, pyrazinyl, triazolyl, thiophenyl, furanyl, quinoliny, purinyl, naphthyl, benzothiazolyl, benzopyridyl, and benzimidazolyl.

10. (Original) A compound of claim 6, wherein at least one of A<sub>1</sub> and A<sub>2</sub> is substituted with at least one and not more than 3 substitution groups.

11. (Original) A compound of claim 10, wherein said substitution groups are independently selected from the group consisting of nitro, amino, cyano, halo, thioamido, amidino, oxamidino, alkoxyamidino, imidino, guanidino, sulfonamido, carboxyl, formyl, loweralkyl, haloloweralkyl, loweralkoxy, haloloweralkoxy, loweralkoxyalkyl, loweralkylaminoloweralkoxy, loweralkylcarbonyl, loweralkylcarbonyl, lowerheteroalkylcarbonyl, alkylthio, aminoalkyl and cyanoalkyl.

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1420 Fifth Avenue  
Suite 2800  
Seattle, Washington 98101  
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12. (Original) A compound of claim 8 wherein A<sub>1</sub> has the formula:



(II)

wherein R<sub>8</sub> and R<sub>9</sub> are independently selected from the group consisting of hydrogen, hydroxy, nitro, amino, cyano, halo, thioamido, amidino, oxamidino, alkoxyamidino, imidino, guanidiny, sulfonamido, carboxyl, formyl, loweralkyl, aminoloweralkyl, loweralkylaminoloweralkyl, haloloweralkyl, loweralkoxy, haloloweralkoxy, loweralkoxyalkyl, loweralkylaminoloweralkoxy, loweralkylcarbonyl, loweralkylcarbonyl, lowerheteroalkylcarbonyl, alkylthio, aryl and, aralkyl.

13. (Original) A compound of claim 12, wherein A<sub>1</sub> is selected from the group consisting of aminopyridyl, nitropyridyl, aminonitropyridyl, cyanopyridyl, cyanothiazolyl, aminocyanopyridyl, trifluoromethylpyridyl, methoxypyridyl, methoxynitropyridyl, methoxycyanopyridyl and nitrothiazolyl.

14. (Original) A compound of claim 1, wherein at least one of R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> is substituted loweralkyl selected from the group consisting of haloloweralkyl, heterocycloaminoalkyl, and loweralkylaminoloweralkyl.

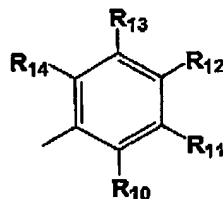
15. (Original) A compound of claim 14, wherein at least one of R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> is loweralkylaminoloweralkyl.

16. (Original) A compound of claim 14, wherein R<sub>1</sub>, R<sub>2</sub>, and R<sub>3</sub> are hydrogen and R<sub>4</sub> is selected from the group consisting of hydrogen, methyl, ethyl, aminoethyl, dimethylaminoethyl, pyridylethyl, piperidinylethyl, pyrrolidinylethyl, piperazinylethyl and morpholinylethyl.

17. (Original) A compound of claim 1, wherein at least one of R<sub>5</sub>, R<sub>6</sub> and R<sub>7</sub> is selected from the group consisting of substituted and unsubstituted aryl, heteroaryl and biaryl.

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1420 Fifth Avenue  
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18. (Original) A compound of claim 17 wherein at least one of R<sub>5</sub>, R<sub>6</sub> and R<sub>7</sub> is a substituted or unsubstituted moiety of the formula:



wherein R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub>, R<sub>13</sub>, and R<sub>14</sub> are independently selected from the group consisting of hydrogen, nitro, amino, cyano, halo, thioamido, carboxyl, hydroxy, and optionally substituted loweralkyl, loweralkoxy, loweralkoxyalkyl, haloloweralkyl, haloloweralkoxy, aminoalkyl, alkylamino, alkylthio, alkylcarbonylamino, aralkylcarbonylamino, heteroaralkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino aminocarbonyl, loweralkylaminocarbonyl, aminoaralkyl, loweralkylaminoalkyl, aryl, heteroaryl, cycloheteroalkyl, aralkyl, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, arylcarbonyloxyalkyl, alkylcarbonyloxyalkyl, heteroarylcarbonyloxyalkyl, aralkylcarbonyloxyalkyl, and heteroaralkylcarbonyloxyalkyl.

19. (Original) A compound of claim 18 wherein R<sub>10</sub>, R<sub>11</sub>, R<sub>13</sub>, and R<sub>14</sub> are hydrogen and R<sub>12</sub> is selected from the group consisting of halo, loweralkyl, hydroxy, loweralkoxy, haloloweralkyl, aminocarbonyl, alkylaminocarbonyl, morpholino, piperidino and cyano.

20. (Original) A compound of claim 18 wherein R<sub>11</sub>, R<sub>13</sub>, and R<sub>14</sub> are hydrogen and R<sub>10</sub> and R<sub>12</sub> are independently selected from the group consisting of halo, loweralkyl, hydroxy, loweralkoxy, haloloweralkyl, morpholino, piperidino and cyano.

21. (Original) A compound of claim 18 wherein R<sub>10</sub>, R<sub>11</sub>, R<sub>13</sub>, and R<sub>14</sub> are hydrogen and R<sub>12</sub> is heteroaryl.

22. (Original) A compound of claim 18 wherein R<sub>10</sub>, R<sub>11</sub>, R<sub>13</sub>, and R<sub>14</sub> are hydrogen and R<sub>12</sub> is a heterocycloalkyl.

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1420 Fifth Avenue  
Suite 2800  
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23. (Original) A compound of claim 18 wherein at least one of R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub>, R<sub>13</sub>, and R<sub>14</sub> are halo and the remainder of R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub>, R<sub>13</sub>, and R<sub>14</sub> are hydrogen.

24. (Original) A compound of claim 18 wherein at least one of R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub>, R<sub>13</sub>, and R<sub>14</sub> are selected from the group consisting of morpholino, piperidino, and the remainder of R<sub>10</sub>, R<sub>11</sub>, R<sub>12</sub>, R<sub>13</sub>, and R<sub>14</sub> are hydrogen.

25. (Original) A compound of claim 18 wherein at least one of R<sub>5</sub>, R<sub>6</sub> and R<sub>7</sub> is selected from the group consisting of dichlorophenyl, difluorophenyl, trifluoromethylphenyl, chlorofluorophenyl, bromochlorophenyl, bromofluorophenyl, ethylphenyl, methylchlorophenyl, ethylchlorophenyl, imidazolylphenyl, cyanophenyl, morpholinophenyl and cyanochlorophenyl.

26. (Original) A compound of claim 1, wherein R<sub>6</sub> is substituted alkyl selected from the group consisting of aralkyl, hydroxyalkyl, aminoalkyl, aminoaralkyl, carbonylaminoalkyl, alkylcarbonylaminoalkyl, arylcarbonylaminoalkyl, aralkylcarbonylaminoalkyl, aminoalkoxyalkyl and arylaminoalkyl.

27. (Original) A compound of claim 1, wherein R<sub>6</sub> is substituted amino selected from the group consisting of alkylamino, alkylcarbonylamino, alkoxycarbonylamino, arylalkylamino, arylcarbonylamino, alkylthiocarbonylamino, arylsulfonylamino, heteroarylamino, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, aralkylcarbonylamino, and heteroaralkylcarbonylamino.

28. (Original) A compound of claim 1, wherein R<sub>6</sub> is selected from the group consisting of unsubstituted or substituted aminocarbonyl, alkyloxycarbonyl, aryloxycarbonyl, aralkyloxycarbonyl and alkylaminoalkyloxycarbonyl.

29. (Original) A compound of claim 1, wherein R<sub>6</sub> is selected from the group consisting of amidino, guanidino, cycloimido, heterocycloimido, cycloamido, heterocycloamido, cyclothioamido and heterocycloloweralkyl.

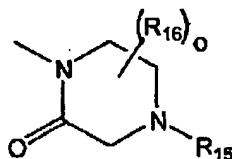
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30. (Original) A compound of claim 1, wherein  $R_6$  is aryl.

31. (Original) A compound of claim 1, wherein at least one of  $R_5$ ,  $R_6$  and  $R_7$  is a substituted or unsubstituted heteroaryl or heterocyclyl group.

32. (Original) A compound of claim 31, wherein at least one of  $R_5$ ,  $R_6$  and  $R_7$  is selected from the group consisting of substituted or unsubstituted pyridyl, pyrimidinyl, pyrrolidinyl, pyrrolinyl, pyrazinyl, thiazolyl, indolyl, imidazolyl, imidazolidinyl, oxadiazolyl, oxazolidinyl, oxazolidinonyl, tetrazolyl, pyrazinyl, pyrazolidinyl, piperidyl, piperazinyl, morpholiny, triazolyl, thienyl, furanyl, quinoliny, pyrrolylpyridyl, pyrazolonyl, pyridazinyl, benzothiazolyl, benzopyridyl, benzotriazolyl, and benzimidazolyl.

33. (Original) A compound of claim 32 wherein at least one of  $R_5$ ,  $R_6$  and  $R_7$  is a monoketopiperazinyl group having the structure:



(IV)

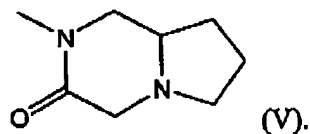
wherein  $R_{15}$  and  $R_{16}$  are independently selected from the group consisting of hydrogen, loweralkyl, loweralkynyl, aryl, heteroaryl, arylloweralkyl, loweralkylarylloweralkyl, haloloweralkyl, haloarylloweralkyl carbocyclic and heterocyclic; or  $R_{16}$  can be taken with another  $R_{16}$  or with  $R_{15}$  to form a carbocyclic, heterocyclic or aryl ring; and  $o$  is an integer between 1 and 3.

34. (Original) A compound of claim 33, wherein  $R_{15}$  is loweralkyl

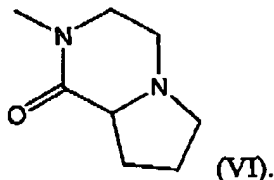
35. (Original) A compound of claim 34, wherein  $R_{15}$  is selected from the group consisting of methyl, ethyl, n-propyl, isopropyl, cyclopropyl, n-butyl, iso-butyl and t-butyl.

36. (Original) A compound of claim 33, wherein  $R_{15}$  is taken with  $R_{16}$  to form a group having the structure:

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1420 Fifth Avenue  
Suite 2800  
Seattle, Washington 98101  
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37. (Original) A compound of claim 33, wherein R<sub>15</sub> is taken with R<sub>16</sub> to form a group having the structure:



38. (Original) A composition comprising an amount of a compound of claim 1 effective to modulate GSK3 activity in a human or animal subject when administered thereto, together with a pharmaceutically acceptable carrier.

39. (Original) A method of inhibiting GSK3 activity in a human or animal subject, comprising administering to the human or animal subject a composition of claim 33.

40. (Original) A method of treating a cell comprising administering to the cell an amount of a compound of claim 1 effective to inhibit GSK3 activity in the cell.

41. (Original) A method for treating a GSK3-mediated disorder in a human or animal subject, comprising administering to the human or animal subject an amount of a composition of claim 38 effective to inhibit GSK3 activity in the subject.

42. (Original) A method of claim 41, wherein the composition is administered by a mode of administration selected from the group consisting of oral, subcutaneous, transdermal, transmucosal, iontophoretic, intravenous, intrathecal, buccal, sublingual, intranasal, and rectal administration.

43. (Original) A method of claim 41, wherein said GSK3-mediated disorder is selected from the group consisting of diabetes, Alzheimer's disease, Parkinson's disease,

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1420 Fifth Avenue  
Suite 2800  
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Huntington's disease, obesity, atherosclerotic cardiovascular disease, essential hypertension, polycystic ovary syndrome, syndrome X, ischemia, traumatic brain injury, bipolar disorder, immunodeficiency and cancer.

44. (Original) A method of claim 43, which further comprises administering to the subject one or more additional active agents.

45. (Original) A method of claim 45, wherein the GSK3-mediated disorder is diabetes and the additional active agent is selected from the group consisting of insulin, troglitazone, rosiglitazone, pioglitazone, glipizide and metformin.

46-47. (Canceled)

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1420 Fifth Avenue  
Suite 2800  
Seattle, Washington 98101  
206.682.8100